UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/706,691	11/12/2003	Andrew Robert Davids	674582-2001	5783

20999 7590 09/23/2005

FROMMER LAWRENCE & HAUG
745 FIFTH AVENUE- 10TH FL.
NEW YORK, NY 10151

EXAMINER	
LEE, BETTY L	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 09/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/706,691	DAVIDS ET AL.	
	Examiner	Art Unit	
	Betty Lee, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,10-16,20 and 21* is/are pending in the application.

4a) Of the above claim(s) *4-9,17-19 and 22-77* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,10-16,20 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/22/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

SDO

DETAILED ACTION

Response to Arguments

Applicant's response filed June 8, 2005 is acknowledged. Applicant's election of Group I, claims 1-3, 10-16, 20 and 21 with traverse is noted. Applicant argues that groups classified under the same class and subclass would not be an undue burden to search. Applicant's arguments have been fully considered but they are not deemed persuasive. The inventions are separate because the search for one protein or polynucleotide sequence is different from the search of a second protein or polynucleotide sequence. It involves comparing the sequence of one SEQ ID with millions of sequences from numerous databases. These searches are not co-extensive and present an undue search burden on the Examiner. The requirement is still deemed proper and is therefore made FINAL. Claims 1-77 are pending. Claims 4-9, 17-19 and 22-27 are withdrawn from consideration as directed to a non-elected invention. Claims 1-3, 10-16, 20 and 21 are under examination.

Claim Objections

1. Claim 15 is objected to as containing non-elected subject matter. The claim encompasses nonelected species.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-3, 10, 11, 15,16 are rejected under 35 U.S.C. 101 because the claims read on a product found in nature. Products of nature e.g. polypeptides, do not constitute patentable subject matter. See MPEP 2105. The polypeptide is a product of nature as evidenced by WO0240671. Human immunoglobin superfamily protein-4 (IGSFP-4) shows 100% homology with SEQ ID16 from 1-240 a.a. Claims 10 and 11 read on naturally occurring antibodies and therefore, products of nature. Examiner suggests the use of the term 'isolated' before polypeptide and antibody.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3,11-13, 15,16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the full length polypeptides of SEQ ID NOs: 16, 26, 20 and 22 and isolated antibodies which specifically bind the full length polypeptide, does not reasonably provide enablement for fragments, other polypeptides having an antigenic determinant in common with SEQ ID NOs: 16, 26, 20 or 22 or functional equivalents thereof, and antibodies which specifically bind the fragments and equivalents. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Additionally, the courts have determined that "... where a statement is, on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977) and have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986).

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and

8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The instant disclosure fails to meet the enablement requirement for the following reasons:

The nature of the invention: The claimed invention is drawn to the polypeptides of SEQ ID NOs: 16, 26, 20 or 22; fragments; polypeptides with an antigenic determinant in common with; and functional equivalents thereof; and to antibodies which bind the polypeptide.

The state of the prior art and the predictability or lack thereof in the art: The art teaches that substitution of as little as a single amino acid will alter protein function (Ju, *et al* PNAS 88-2658-2662, 1991). For example, Ju *et al* (PNAS 88:2658-2662, 1991) teach that substitution of Lys-145 to Asp will convert the IL-1 receptor antagonist into an agonist. Lederman, *et al* (Mol. Immunol. 28(11):1171-81,1991) teach that a arginine-tryptophan substitution at amino acid 240 of the CD4 molecule abolishes the binding of the monoclonal antibody OKT4.

The amount of direction or guidance present and the presence or absence of working examples: The specification does not disclose the functional domains which are required for functional equivalents and does not disclose the structures that are important for retention of polypeptide activity. The specification fails to provide any guidance as to how to make or use 'fragments' or mutated polypeptides with similar antigenic determinants which retain the function of the full length polypeptide. There are no working examples directed to any mutated polypeptides or fragments which retain

the activity of the full length polypeptide. There are no working examples directed to antibodies, which were made against any mutant polypeptides or fragments. In fact, the working examples are limited to making the full length polypeptide and to administration of that polypeptide in a mouse model for treating hepatitis.

The breadth of the claims and the quantity of experimentation needed: The claims are directed to a broad spectrum of fragments and variants having the same activity as the full length polypeptides of SEQ ID NOs: 16, 26, 20 or 22. However since the art teaches that there is considerable unpredictability in retaining protein function even with a single amino acid substitution, it would require undue experimentation for a person of skill in the art to be able to use the invention as described.

4. Claims 15,16, 20 and 21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating hepatitis in a mouse model comprising administration of INSP052 (SEQ ID NO: 16) or INSP052EC (SEQ ID NO: 20 or 22) protein by injection, does not reasonably provide enablement "for treating or diagnosing all diseases " by administering a polypeptide of SEQ ID NO: 20 or 22 (the INSP052EC protein), a nucleic acid molecule encoding the protein, a ligand that binds the protein, or a compound that modulates the activity of the protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The nature of the invention: The claimed invention is drawn to the polypeptides of SEQ ID NOs: 16, 26, 20 or 22, to nucleic acid molecules encoding the polypeptides, to

ligands which bind the polypeptides and to compounds which modulate the level of expression or activity of the polypeptides for use in diagnosis or therapy of disease. Thus, therapeutic administration is encompassed within the claimed invention. The specification (pg 16-17) teaches the diseases which may be treated according to the claimed method as including cell proliferative disorders, autoimmune/inflammatory disorders, cardiovascular disorders, neurological and psychiatric disorders, developmental disorders, metabolic disorders, infections, pathological conditions, cancer, AIDS, Alzheimer's disease, brain/spinal cord injury, Crohn's disease and inflammatory bowel disease.

The state of the prior art and the predictability or lack thereof in the art: The art teaches that the pathology of the recited diseases is varied and not necessarily due to altered cytokine levels. For example, familial hypercholesterolaemia (FH) affects about 10 million people in the world and is characterized by elevated serum cholesterol (Marks, *et al* Atherosclerosis 168:1-14, 2003). Marks, *et al* teach that the majority of cases of FH are due to one of many different mutations of the low density lipoprotein (LDL) receptor and more than 700 different mutations have been reported world-wide (pg 3, col 2, lines 52-54 and pg 4 col 1, line 1). Different mutations have different effects on LDL receptor function that may result in severe clinical consequences. Therefore, the art teaches a high degree of unpredictablilty in etiology of the recited diseases and teaches that they are not necessarily related to altered cytokine levels but rather may be due to very different causes, such as genetic mutations of specific gene(s).

The amount of direction or guidance present and the presence or absence of working examples: Given the teachings of the art that diseases such as FH are due to factors other than altered cytokine levels, detailed teachings must be present in the specification to overcome the teachings of unpredictablility found in the art. These teachings are absent. The specification describes the *in vivo* administration of the extracellular domain of INSP052 cDNA (encoding the polypeptide of SEQ ID NO: 20 or 22) to a mouse model with hepatitis and the resulting effects of decreasing TNF-alpha and IL-6 levels in serum. The specification provides no guidance as to how to treat or diagnose diseases in general other than hepatitis by using the claimed polypeptides. There is a single working example (page 72-74) which is directed to treating hepatitis in a mouse model. There are no working examples directed to treating any diseases other than hepatitis.

The breadth of the claims and the quantity of experimentation needed: The claims are broadly drawn to treating cancer, autoimmune diseases, neurological diseases, genetic diseases, infections, liver disease, AIDS, Parkinson's disease, renal disease, etc. The art teaches a high level of unpredictability in the diagnosis and the treatment of this broad range of diseases. The specification fails to overcome the teachings of unpredictability in the art. Therefore, it would require undue experimentation by one of skill in the art to practice the invention commensurate in scope with the claims.

5. Claims 10-16, 20 and 21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a written description rejection, rather than an enablement rejection under 35 U.S.C. 112, first paragraph. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, & 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Vas-Cath Inc. V. Mahurka, 19 USPQ2d 1111, states that applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the written description inquiry, is *whatever is now claimed* (see page 1117). A review of the language of the claim indicates that these claims are drawn to a genus, i.e., full length polypeptides comprising SEQ ID NOs: 16, 26, 20 and 22, fragments and functional equivalents of SEQ ID NOs: 16, 26, 20 and 22; and to antibodies which bind to the full length polypeptides, fragments thereof and functional equivalents of SEQ ID NOs: 16, 26, 20 and 22.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a

substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In *Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus. At section B(1), the court states An adequate written description of a DNA ... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention.

There are four species of the claimed genus disclosed that are within the scope of the claimed genus, *i.e. the full length polypeptides of SEQ ID NO: 16, 26, 20 and 22.* The disclosure of even a single species may provide an adequate written description of a genus when the species disclosed is representative of the genus. However, the present claims encompass numerous species that are not further described; fragments, functional equivalents and antibodies directed against the polypeptides, functional equivalents and fragments. There is substantial variability among the species.

One of skill in the art would not recognize from the disclosure that the applicant was in possession of the genus of which comprises a broad range of full length polypeptides comprising SEQ ID NOs: 16, 26, 20 and 22, fragments and functional

equivalents thereof; and antibodies which bind to full length polypeptides, fragments and functional equivalents of SEQ ID NOs: 16, 26, 20 and 22.

The specification does not clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed (see *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 10-16, 20 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "antigenic determinant" is not defined in the specification. Absent specific delineation of the term, the metes and bounds of the claimed invention cannot be determined and the claims are indefinite.

Claims 12-15 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase 'increases or decreases the level of expression or activity of a polypeptide' is indefinite because the claim does not specify what the level is compared to.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1,2,3,10-16, 20 and 21 are rejected under 35 U.S.C. 102(e) as being anticipated by Baughn, *et al* (WO0240671).

The claimed invention is drawn to a polypeptide of SEQ ID NOs: 16, 26, 20 or 22, fragments, polypeptides with an antigenic determinant in common with, and functional equivalents thereof for use in treating or diagnosing disease. The claimed invention is also drawn to ligands (or antibodies), which specifically bind and inhibit the activity of the polypeptide and to compounds that increase or decrease the level of expression or activity of the polypeptide.

Baughn, *et al* teaches a human immunoglobin superfamily protein-4 (IGSFP-4) that is useful for diagnosing and treating immune or cell proliferative diseases, including hepatitis. The IGSFP-4 disclosed by Baughn, *et al* shows 100% homology with instant SEQ ID No.16 from aa1-240. Baughn, *et al* teach (on pg 39, lines 21-23) that IGSFP can be used to screen peptide libraries for inhibitors. Baughn, *et al* further teach (on pg

40, lines 8-14), that IGSFP can be used to screen for compounds including antibodies, ligands, and structural or functional mimetics that bind specifically to IGSFP. Baughn, *et al* further teach that IGSFP can be used to screen for compounds, which include agonists and antagonists, that modulate its activity (pg 40, lines 30-33 and pg 41, lines 1-7). Baughn, *et al* teach that IGSFP, or fragments or derivatives thereof, may be administered to a subject to treat disorders associated with decrease expression or activity of IGSFP (pg 42, lines 13-15). Similarly, the proposed therapeutic and diagnostic uses for ligands that inhibit the activity of and compounds that affect the level of expression of the claimed polypeptides are anticipated by Baughn, *et al* because they teach that 'any of the proteins, antagonists, antibodies, agonists, complementary sequences or vectors of the invention may be administered in combination with other appropriate therapeutic agents' (pg 44, lines 22-28). Finally, Baughn, *et al* teach the use of IGSFP as a diagnostic tool for diseases associated with altered levels of IGSFP (pg 55, lines 14-33 and pg 56, lines 1-2).

8. Claims 1-3, and 12-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Edwards, *et al* (US Patent 6783961).

The claimed invention is drawn to a polypeptides of SEQ ID NOs: 16, 26, 20 and 22, fragments, polypeptides with an antigenic determinant in common with, and functional equivalents thereof for use in treating or diagnosing disease.

Edwards, *et al* teach a protein with 100% homology to SEQ ID NO: 16 from aa 1-58 (see col 60, lines 19-28). Edwards, *et al* teach that the protein can be used to treat inflammatory bowel disease characterized by an overexpression of cytokines such as

TNF or IL-1. Absent evidence to the contrary, the polypeptide taught by Edwards, *et al* would be expected to have the same activity as the polypeptide of SEQ ID NO: 16 of the instant application to increase its activity by synergistically enhancing its effect on cytokine expression. The polypeptide of Edwards, *et al* would meet the limitations of "a compound that increases or decreases the level of expression or activity of the claimed polypeptide". Lastly, because the polypeptide taught by Edwards, *et al* occurs as a natural product, it would meet the limitation of "a natural substrate or functional mimetic" of SEQ ID No. 16.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Betty Lee, Ph.D. whose telephone number is (571) 272-8152. The examiner can normally be reached on M-F 9 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BLL

Brenda Brumback

BRENDA BRUMBACK
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600